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## OBSERVATIONS ON THE PHAGOCYTTIC ACTIVITY OF THE LEUKOCYTES IN MEASLES.\*

RUTH TUNNICLIFF.

*(From the Memorial Institute for Infectious Diseases, Chicago.)*

Observations have been made on the blood of six measles patients to determine whether any changes occur in the phagocytic activity of the leukocytes during the leukopenia. Suspensions of washed blood, containing approximately the same number of polymorphonuclear neutrophils from normal persons and from cases of measles were used. The phagocytic activity of the leukocytes was determined by comparing the number of bacteria ingested by the two sets of leukocytes under the influence of normal serum (cytophagic index). At the same time the opsonic index of the measles patients was estimated in the usual way. Typical strains of the streptococcus pyogenes, the staphylococcus aureus, and the tubercle bacillus were employed in these experiments.

In the case of all the patients examined during the leukopenia, the polymorphonuclear cells were found to be less actively phagocytic than normal cells, the average for the streptococcus being 0.53, the staphylococcus 0.6, and the tubercle bacillus 0.54, as compared with the normal standard of 1.00. In three cases examined when the number of leukocytes had become normal, the neutrophils were found to be normally active. In one of these cases there was on the seventh day of the attack a leukocytosis, at which time the neutrophils were more actively phagocytic. The patient had a bronchitis, which perhaps accounted for the large number of leukocytes (21,000).

The opsonic index was found to be normal except in two cases in which the streptococcus index was low. In one case examined at the end of the acute attack, the streptococcus index was slightly increased (1.4).

In order to determine whether this change in the activity of

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the leukocytes also occurs in experimental measles, a monkey (*Macacus rhesus*) was inoculated with measles blood and the opsonic index, and the cytophagic index to the streptococcus, the staphylococcus, and the tubercle bacillus estimated at frequent intervals. The blood was obtained from an adult woman, 24 hours after the appearance of a typical measles rash. Five cubic centimeters of blood were withdrawn from the elbow and mixed with eight cubic centimeters of citrate-salt solution (1 per cent sodium citrate in physiological salt solution). One-half of this mixture was injected intravenously and the other half intraperitoneally, about thirty minutes after the withdrawal of the blood.

At the time of the inoculation the temperature of the monkey was  $104^{\circ}$ . It gradually fell to  $102.6^{\circ}$  on the seventh day after inoculation. On the eighth day, it rose to  $103.5^{\circ}$ , falling slightly the following day, and remaining at that point during the remainder of the experiment. It is possible that the rise in the temperature on the eighth day may have been due to the measles virus.

On the seventh day the mucous membranes of the mouth appeared redder than usual, but no typical Koplik spots could be demonstrated. Twelve days after the inoculation the monkey appeared a little sick. No rash could be seen at any time.

The number of leukocytes was not increased after the injection of measles blood, but on the fifth day there commenced a distinct fall in the total number of leukocytes, lasting for 15 days. On the 22d day there was a slight leukocytosis, the number falling to normal the following day and remaining there subsequently.

The total number of neutrophils was increased for two days following the injection, then fell below normal for 15 days, increasing again on the 21st day. The total number of lymphocytes (Chart 1) decreased on the day following the inoculation and remained low for 16 days and then returned to normal. The large mononuclear cells (Chart 1) were slightly increased on the fifth day and then remained normal during the remainder of the experiment.

The phagocytic activity of the neutrophils (Chart 2) for the streptococcus, staphylococcus, and the tubercle bacillus was increased on the third day following the injection of measles blood.

At this time the total number of polymorphonuclear neutrophils was increased. With the onset of the leukopenia the neutrophils became less actively phagocytic, not returning to their normal activity until the leukopenia ceased on the 22d day. No increased activity was observed at the end of the reaction.

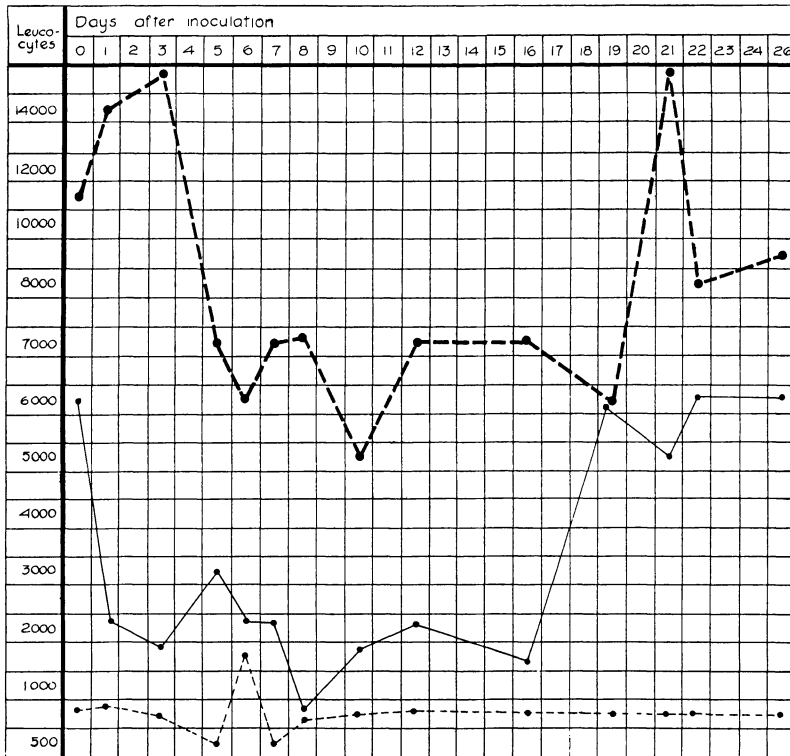


CHART 1.—Leukocyte curves in *Macacus rhesus* inoculated intravenously and intraperitoneally with 5 c.c. measles blood.

Heavy broken line = Total number of polymorphonuclear neutrophils.

Fine broken line = Total number of large mononuclears.

Fine solid line = Total number of lymphocytes.

The opsonic index to the staphylococcus and tubercle bacillus remained about normal after the inoculation of the measles blood, but the streptococcus index rose on the third day to 1.5 and then fell below normal on the sixth day, not returning to normal until the 20th day. It is of interest to note that the patient from whom this blood was taken had a low streptococcus index throughout the

course of her infection. Just what significance this low streptococcus index might have, could not be determined.

On account of the few clinical symptoms exhibited by the monkey injected with measles blood, another monkey was inoculated with normal blood to determine whether it would produce a leukopenia and with it a decreased activity of the leukocytes.

A monkey (*Macacus rhesus*) was injected with six cubic centimeters of normal blood, mixed with eight cubic centimeters of citrate-salt solution, one-half intraperitoneally and one-half in-

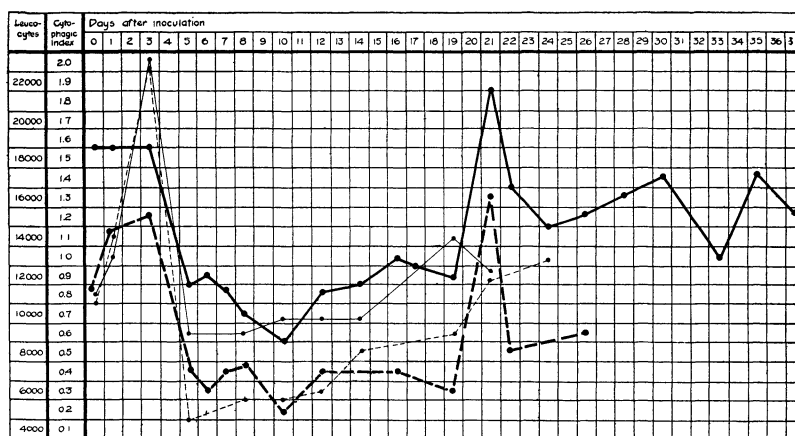


CHART 2.—Phagocytic activity of leukocytes in *Macacus rhesus* inoculated intravenously and intraperitoneally with 5 c.c. of measles blood.

Heavy solid line = Total number of leukocytes.

Heavy broken line = Total number of polymorphonuclear neutrophils.

Fine solid line = *Staphylococcus* cytophagic index.

Fine broken line = *Streptococcus* cytophagic index.

travenously. There was no change in the temperature, and the monkey remained perfectly well. A slight increase in the number of leukocytes followed the injection, but no leukopenia occurred. The total number of neutrophils was increased after the injection, but no greater change occurred in the number of lymphocytes and large mononuclears than occurred before the inoculation.

The phagocytic activity of the leukocytes was not affected by the injection of normal blood, the variations being within the limits of experimental error. No changes were observed in the opsonin.

Although this monkey had fewer leukocytes before the injection than the measles monkey, and the proportion of lymphocytes and neutrophiles was more nearly equal than in the measles monkey, it seems fair to assume that the leukopenia and decrease in phagocytic activity of the leukocytes produced in the monkey injected with measles blood was due to the measles virus and not altogether to the human blood.

The results of the observations on the number of leukocytes differ from those of Hektoen and Eggers and from some of those of Lucas and Prizer, in that I found no initial leukocytosis after the inoculation of measles blood.

Hektoen and Eggers<sup>1</sup> found that in measles in the monkey the leukocytes appear to behave very much as they do in human measles; that is, that preceded by a more or less distinct leukocytosis there occurs a leukopenia of variable degree in what would correspond in a general way to the latter part of the pre-eruptive and early part of the eruptive periods. In their animals, the leukopenia involved principally the neutrophiles, the lymphocytes being relatively somewhat increased.

Lucas and Prizer<sup>2</sup> observed that during the pre-eruptive stage of measles in *Macacus rhesus*, there is a leukopenia involving the polymorphonuclear neutrophiles. This leukopenia develops in from five to 10 days after the inoculation and may be preceded by a transient lymphocytic and large mononuclear leukocytosis which is probably absent or only poorly developed in the severe form of the reaction but is strongly developed in the less severe cases.

#### CONCLUSIONS.

From these experiments the following conclusions may be drawn:

1. The phagocytic activity of the leukocytes is decreased for the streptococcus, staphylococcus, and tubercle bacillus during the leukopenia of measles in man. Their activity becomes normal with the increase in their number.
2. The inoculation of the monkey (*Macacus rhesus*) with measles blood is followed by a leukopenia involving the polymorphonuclear

<sup>1</sup> *Jour. Am. Med. Assoc.*, 1911, 57, p. 1833.

<sup>2</sup> *Jour. Med. Res.*, 1912, 26, p. 181.

neutrophiles and lymphocytes, the large mononuclear cells being slightly increased. The leukopenia is preceded and followed by an increase in the number of neutrophiles.

3. The inoculation of the monkey with measles blood produces at first an increased phagocytic activity of the leukocytes, followed by a decided decrease in their activity with the onset of the leukopenia. This decreased activity persists until the number of leukocytes becomes normal.

4. The injection of normal blood into the monkey produces a slight leukocytosis, but no leukopenia and no change in the phagocytic activity of the leukocytes. The total number of neutrophiles is slightly increased, but no marked changes are observed in the lymphocytes and large mononuclear cells.

Finally I would suggest that the leukopenia and the diminution of the phagocytic activity of the leukocytes in measles may account in some degree for the frequency of secondary infections in this disease.